Journal of Organometallic Chemistry, 99 (1975) 385—389

AZOLE CHEMISTRY

XI*. 3-DIMETHYLSILA-2*H*-IMIDAZO[1,2-*a*]BENZIMIDAZOLES

HOWARD ALPER** and MICHAEL S. WOLIN

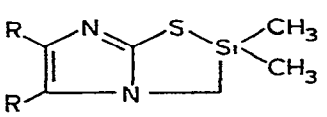
Department of Chemistry, University of Ottawa, Ottawa, Ontario K1N 6N5 (Canada) and Department of Chemistry, State University of New York at Binghamton, Binghamton, New York 13901 (U.S.A.)

(Received April 15th, 1975)

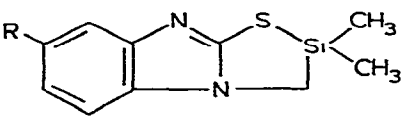
Summary

2-Aminobenzimidazole, and its 5,6-dichloro, 5,6-dimethyl, and 5,6-dinitro derivatives react with bromomethyldimethylchlorosilane in anhydrous tetrahydrofuran at room temperature to give the new heterocycles, 3-dimethylsila-2*H*-imidazo[1,2-*a*]benzimidazoles, in good yields. The spectral properties of these heterocycles are discussed.

A recent paper [1] has reported the condensation of appropriate mercaptazoles with bromomethyldimethylchlorosilane (followed by cyclohydrohalogenation) to give 2-dimethylsila-3*H*-imidazo[2,1-*b*]thiazoles (I) and 2-dimethylsila-3*H*-thiazolo[3,2-*a*]benzimidazoles (II). We now describe the use of bromomethyldimethylchlorosilane in very simple, one-step synthesis of nitrogen azoles containing heterocyclic silicon.



(I)



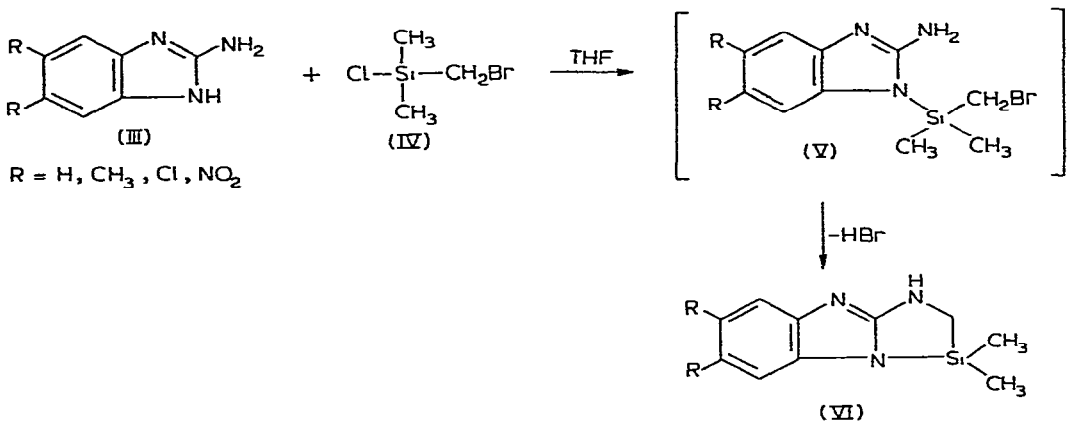
(II)

Treatment of 2-aminobenzimidazole (III, R = H) with bromomethyldimethylchlorosilane (IV) in dry tetrahydrofuran at room temperature gave

* For part X see ref. 1.

** Address correspondence to this author at Ottawa.

3-dimethylsila-2*H*-imidazo[1,2-*a*]benzimidazole (VI, R = H) in 48% yield. Use of the 5,6-dimethyl, 5,6-dichloro, and 5,6-dinitro derivatives of III gave the



corresponding silaazoles VI, R = CH_3, Cl, NO_2 in 68-82% yields. The yields and other pertinent data for VI are listed in Table 1.

The structures of the fused azoles were established on the basis of analytical data and spectral results (Table 1). The infrared spectra (KBr disc) of VI displayed bands at 1430-1435 cm^{-1} and at 1254-1261 cm^{-1}, due to $\delta_{as}(CH_3Si)$ and $\delta_s(CH_3Si)$, respectively. In addition, the sharp, intense stretching vibration of the free amino group of III, which occurs in the region of 3400-3440 cm^{-1}, is replaced by a broad absorption at 3400-2800 cm^{-1} in VI. The dimethylsilyl group of VI gave a singlet signal in the nuclear magnetic resonance spectrum (DMSO-d_6) at δ 0.15-0.19. A singlet was also observed for the methylene protons of VI, (δ 2.44-2.49) and a broad singlet at δ 3.70-3.87 was assgined to the amino proton. The mass spectrum of each of these silicon containing heterocycles exhibited intense molecular ion peaks.

In the synthesis of the parent imidazo[1,2-*a*]benzimidazole system (III used as reactant), it has been shown that condensation occurs at a ring nitrogen of III [2]. It seems reasonable then to expect that the condensation of III with the silyl chloride IV would also occur at a ring nitrogen to give V, which can then eliminate HBr to afford the fused benzimidazole VI. The latter step takes place in the absence of 1,8-bis(dimethylamino)naphthalene, required in the preparation of I and II. This difference between the two systems may be a consequence of the different basicities of the nitrogen atoms involved in the respective cyclodehydrohalogenation steps.

The silicon—nitrogen bond of VI (R = H) was cleaved by excess acetic anhydride [3] to give the *N,N'*-diacetylsilyl carboxylate VII, which was isolated as the siloxane, VIII by hydrolysis. Two carbonyl stretching bands appeared in

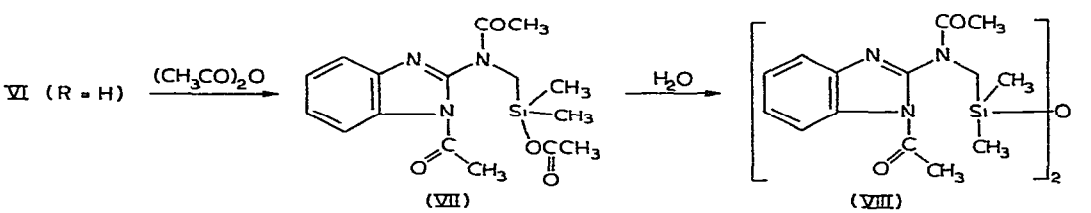


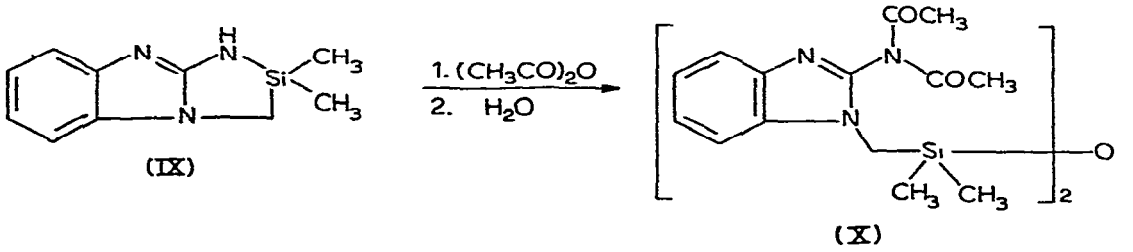
TABLE 1

PERTINENT DATA FOR VI

R	Formula [a]	Yield (%)	M.p. (°C)	IR (KBr) cm^{-1}	NMR (DMSO-d_6) [b] δ (ppm)	Mass spectrum M^+ (m/e)
H	$C_{10}H_{13}N_3Si$	48	62 64	3400-2800 (HN), 1430 (CH_3Si), 1261 (CH_3Si)	0.15 (s, 6H, $Si(CH_3)_2$), 2.48 (s, 2H, CH_2), 3.87 (s, 1H, NH), 7.0-7.5 (m, 4H, aromatic)	203
CH_3	$C_{12}H_{17}N_3Si$	70	123-125	3400-2800 (NH), 1435 (CH_3Si), 1258 (CH_3Si)	0.17 (s, 6H, $Si(CH_3)_2$), 2.22 (s, 6H, CH_3), 2.44 (s, 2H, CH_2), 3.83 (s(br), 1H, NH), 7.12 (s, 2H, aromatic)	231
Cl	$C_{10}H_{11}Cl_2N_3Si$	82	107-109	3400-2800 (NH), 1431 (CH_3Si), 1254 (CH_3Si)	0 19 (s, 6H, $Si(CH_3)_2$) 2.49 (s, 2H, CH_2) 3.70 (s(br), 1H, NH), 7.33 (s, 2H, aromatic)	274
NO_2	$C_{10}H_{11}N_5O_4Si$	68	192-195	3400-2800 (NH), 1432 (CH_3Si), 1257 (CH_3Si)	0.17 (s, 6H, $Si(CH_3)_2$), 2.49 (s, 2H, CH_2), 3.81 (s, 1H, NH), 7.61 (s, 2H, aromatic)	293

[a] All compounds gave C, H, and N analysis within 0.4 of the calculated values. [b] Tetramethylsilane was used as external standard.

the IR spectrum of VIII at 1725 cm^{-1} (acetyl attached to heterocyclic nitrogen) [4] and at 1660 cm^{-1} (other acetyl group). The NMR spectrum displayed two singlet signals at δ 2.25 and δ 2.69 [5], due to the methyl protons of the two acetyl groups. The formation of VIII provides additional support to the structure assigned to VI since the isomer IX would afford X on acetic anhydride cleavage, followed by hydrolysis.



(IX) (X)

In conclusion, the results, obtained herein, as well as those reported previously [1], demonstrate the general utility of bromomethyldimethylchlorosilane as a reagent for the synthesis of novel silicon heterocycles.

The new heterocycles are currently being tested for physiological activity.

Experimental

General

Elemental analyses were determined by Galbraith Laboratories, Inc. Knoxville, Tenn. and by Heterocyclic Chemical Corp., Harrisonville, Missouri. Infrared spectra were recorded on a Perkin—Elmer 457 or Beckman IR 20A spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian T-60 spectrometer. Mass spectra were determined on a Varian MS902 spectrometer.

Bromomethyldimethylchlorosilane was purchased from PCR, Inc., and was used as received. 2-Aminobenzimidazole and 2-amino-5,6-dimethylbenzimidazole were commercial materials (Eastman Organic Chemicals) and were recrystal lized and oven dried prior to use. 2-Amino-5,6-dichlorobenzimidazole (III, R = Cl, m.p. 261-262°C [6]) and 2-amino-5,6-dinitrobenzimidazole (III, R = NO_2, m.p. 314°C dec. [7]) were prepared by treatment of the appropriately substituted *o*-phenylenediamine with cyanogen bromide.

All reactions were run under a nitrogen atmosphere, weighings and reaction-work-ups being carried out in a glove bag.

General procedure for reactions of 2-aminobenzimidazoles (III) with bromomethyldimethylchlorosilane (IV)

A tetrahydrofuran (60-100 ml) solution containing the aminobenzimidazole (III, R = H, CH_3, Cl, NO_2) and bromomethyldimethylchlorosilane (IV, 1.3/1.0 mole ratio of IV/III) was stirred at room temperature for 2-4 days. The reaction mixture was filtered, and addition of pentane to the filtrate deposited a yellow oil. Tetrahydrofuran was removed by decantation and the oil VI solidified on vacuum drying. The product was washed well with cold water, and

then with pentane. Pertinent physical data for these heterocycles are listed in Table 1.

Reaction of VI (R = H) with acetic anhydride

Compound VI, R = H (0.50 g, 2.5 mmol) was dissolved in 50 ml of cold acetic anhydride. After complete dissolution, the solution was heated to 50-55°C for 1 h, cooled to room temperature, and then poured onto crushed ice. The resulting siloxane VIII (0.31 g, 42%) was filtered and dried. IR ($CHCl_3$): ν(CO) 1725, 1660 cm^{-1}, ν(Si—O) 1060 cm^{-1}; NMR ($CDCl_3$): δ 0.17 (s, 6H, $Si(CH_3)_2$), δ 2.25 (s, 3H, $NCOCH_3$), δ 2.69 (s, 3H, heterocyclic $NCOCH_3$), δ 3.15 (s, 2H, CH_2), δ 7.00-7.60 (m, 4H, aromatic protons). Found: C, 57.02; H, 6.04; N, 14.71. $C_{28}H_{36}N_6O_5Si_2$ calcd.: C, 56.73; H, 6.12; N, 14.17%.

Acknowledgements

We are grateful to Bristol Laboratories, and to the National Research Council of Canada, for support of this work.

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